#240

(Cf. #219 & 219A
denied)

TOBACCO INDUSTRY RESEARCH COMMITTEE

150 East Forty Second Street New York 17, N.Y.

Application For Research Grant

Date: July 1, 1959

1. Name of Investigator: Robert H. Linnell

2. Title: Associate Professor of Chemistry

3. Institution & Address: University of Vermont
Burlington, Vermont

4. Project or Subject: The Oxidation of Nicotine by Gaseous Oxygen: Mechanism, Products and Kinetics

5. Detailed Plan of Procedure: Previous work by the applicant (unpublished) indicates that cotinine ((N-methyl-2-(3-pyridyl)-5-pyrrolidone)) is a major product of the O_2 oxidation of nicotine at temperatures near ambient ((see Frankenburg, J.A.C.S. 79 149 (1957))). The reaction may proceed through a nicotine-oxygen complex (pi-electron complex) as is probably the case with pyrrole ((see Linnell, Arch. Biochem. and Biophys. 57 264 (1955))). Low temperature ultraviolet studies will be used to study the nicotine-oxygen complex. Infrared provides a convenient means for analysis of cotinine in the presence of excess nicotine ((See Frankenburg above and Eddy and Eisner, Anal. Chem. 26 1428 (1954))) as well as detection and analysis of other nicotine derivatives. A vacuum system will be built to study oxygen uptake. The Kinetics of the reaction with oxygen will be followed at a series of temperatures, near ambient temperatures. Work now in progress has shown that the oxidation of nicotine at room temperature with air is a free radical reaction which can be inhibited by antioxidants (hindered phenols, "radical traps") and accelerated by typical free radical sources such as AIBN. Reaction products are therefore complex and chromatography will be used to establish the various products.

6. Budget Plan:

Salaries	1575.00
Expendable Supplies	------
Permanent Equipment	400.00
Overhead 15%	325.00
Other (travel)	200.00
Total	$2500.00

7. Anticipated Duration of Work: This grant will be used for the summer of 1959 with other support expected in the fall from the National Science Foundation.

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8. Facilities and Staff Available: A Perkins-Elmer model 112 infrared instrument with both LiF and NaCl optics and associated equipment is available. Glass blowing and conventional laboratory facilities are quite adequate for this study.

9. Additional Requirements: The permanent equipment item is for a thermostat bath, shaking equipment and associated apparatus to measure rates of O_2 uptake in nicotine solutions at a series of temperatures.

10. Additional Information (Including relation of work to other projects and other sources of supply): The project director has his B.S. and M.S. (chemistry) from the Univ. of New Hampshire, and his Ph.D. under Dr. W. A. Noyes at the Univ. of Rochester, and has worked with the physical-organic chemistry of N-heterocyclics (Photo-chemistry: Pyridine-Acetone, J.A.C.S. 73 3986 (1951); Pyridine-Pyrrole H-Bonding, J. Chem. Phys. 21 179 (1953) and ibid. 23 93 (1955); Anabasine, J.A.C.S. 76 1391 (1954); Polarographic Studies on Bi-pyridines, J.A.C.S. 77 6207 (1955); Tetramethyl bipyridine, J. Org. Chem. 22 1691 (1957); other publication in process on The Reaction of Sodium with Pyridine, Pyrolysis of Pyridine, 2,3-Biquinoline, U.V. of N=C-C=N compounds in H_2SO_4.) Currently H-Bonding studies are underway with Pyrrole and various pyridines, using infrared and a series of temperatures so as to evaluate $\Delta F, \Delta H$ and ΔS. This work is supported by Research Corporation.

Obtaining information on nicotine oxidation products and Kinetics would be a step in the direction of further understanding of the complex problems in tobacco technology and in questions involving health.

Signature /s/ Robert H. Linnell
Director of Project

/s/ George N. Clerkin, Treasurer

/s/ Howard M. Smith, Jr.
Sec'y. Division of Research
in the Physical Sciences